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MV

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/191,199	11/12/98	TANG	P 238/130

022249
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HM12/0317

EXAMINER

COLEMAN, B

ART UNIT

PAPER NUMBER

1624

DATE MAILED:

03/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/191,199

Applicant(s)
TANG et al.

Examiner
Brenda Coleman

Group Art Unit
1624



☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9, 11-16, 18-37, and 41-45 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 18 is/are allowed.

☒ Claim(s) 1-9, 11-16, 19-37, and 41-45 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5, 6, 8, 9

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1624

DETAILED ACTION

Claims 1-9, 11-16, 18-37 and 41-45 are pending in the application.

Election/Restriction

1. Applicant's election with traverse of Group I in Paper No. 13 is acknowledged. The traversal is on the ground(s) that it would not be a burdensome search. This is not found persuasive because first a heterocyclic moiety having a bicyclic ring system with nine ring atoms where at least one is a nitrogen atom is clearly a structurally dissimilar compound which is classified in various subclasses under classes 544 and 546 with respect to the number and position of the nitrogen atoms for which D, E, F and G may contain.

(1) Note MPEP 2173.05(h) "where a Markush expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by a consideration of the compound as a whole, and does not depend on there being a community of properties in the members of the Markush expression.

Therefore, what should be considered for patentable distinctness is the compound as a whole. Would a whole compound where D and F are nitrogen be patentably distinct from a whole compound where D is nitrogen? If a reference for one would not be a reference for the other, then restriction is considered proper. Community of properties is not enough to keep 5,7-diaza-indoline and 4-aza-indoline in the same Markush claim, where the Markush expression is applied only to a portion of a chemical compound. It is the compound as a whole 5,7-

Art Unit: 1624

diazaindoline vs 4-aza-indoline vs 7-aza-indoline, etc., that must be considered for patentable distinctness.

Thus, separate searches in the literature would be required. However, should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

(2) The degree of burden on the examiner is high. The class/subclass search on the elected invention where the compounds of formula I are an aza-indoline core would be as follows: class 514, subclass 300 and class 546, subclass 113 which involved 724 US patents. The classes and subclass mentioned above represent only the degree of burden within the U.S. Patent Classification System, this does not include the search required in the prior art of journal articles and foreign patents.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

2. The information disclosure statement filed May 3, 1999 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be

Art Unit: 1624

listed. It has been placed in the application file, but the information referred to therein has not been considered. The French (AJ) and Hungarian (AK) patents were not available nor was the Beilstein Reg. No. 252929 labeled AT.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The variable Z can be sulfur and NR¹¹ as well as oxygen.

4. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

5. The examiner cannot understand the invention because certain portions of the disclosure are illegible. The illegible portion(s) consist of pages 41-54.

Art Unit: 1624

Applicant is required to submit an appropriate amendment rectifying this deficiency. In the alternative, a substitute specification under 37 CFR 1.125(b) may be filed. The substitute specification must be accompanied by: (1) a statement that the substitute specification contains no new matter; and (2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

6. When a non-provisional application is entitled to an earlier U.S. effective filing date of one or more provisional applications under 35 U.S.C. 119(e), a statement such as "This application is a continuation-in-part of U.S. Application No. 09/096,014 filed June 10, 1998, which claims the benefit of U.S. Provisional Application No. 60/049,324 filed June 11, 1997, and U.S. Provisional Application No. 60/059,381, filed September 19, 1997. should appear as the first sentence of the description.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-9, 11-16, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of "prodrug" is not adequately enabled. Applicants provide

Art Unit: 1624

no guidance as how the compounds are made more active *in vivo*. The choice of a “prodrug” will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrug will be suitable for the instant invention.

8. Claims 21-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims are not adequately enabled solely based on its protein tyrosine kinase inhibition provided in the specification. Instant claim language embraces disorders not only for treatment but for **prevention** which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop lung cancer, prostate cancer, astrocytoma, breast cancer, etc. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-9, 11-16, 19-37 and 41-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

Art Unit: 1624

- a) Claims 1-9, 11-16, 19-37 and 41-45 are vague and indefinite in that many of the substituents for R^{11} , R^1 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{12} and R^{13} are not valence satisfied and/or defined as such in the specification that they include variables which are not defined within the claim, i.e. C-carboxyl, O-carboxyl, C-amido, guanyl, sulfonyl, **etc.** Emphasis added because for some of the variables these are not the only ones or those listed are more than is defined for some variables.
- b) Claims 1 and 41 are vague and indefinite in that it is not known what is meant by O-thiocarbamyl, since thiocarbamyl does not contain an O atom.
- c) Claim 16 recites the limitation "trihalomethane-carbonyl" in the definition of R^4 , R^5 and R^6 . There is insufficient antecedent basis for this limitation in the claim.
- d) Claims 19, 20 and 41 are dependent upon canceled claims 10 and 17.
- e) Claim 20 indicates "comprising administering a therapeutically effective amount" which is unclear as to whether this is indicative of a subject in need thereof.
- f) Claims 42 and 43 are vague and indefinite in that "the compounds listed in Table 1" does not permit claims 42 and 43 to stand on their own, thus describing within the claim that which is being claimed.
- g) Claim 33 is vague and indefinite in that it is not known what is meant by "met related disorder".

Art Unit: 1624

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-5, 9, 11, 12, 16, 19-37 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al., WO 96/16964 (US equivalent 5,719,135). The generic structure of US '135 encompasses the instantly claimed compounds (see Formula I, column 1) and for the same use (see column 11, lines 24+) as claimed herein. Examples 53-71, etc. differ only in the nature of the R₁, R₂, R₃, q and A substituents. Column 1, lines 23 through column 2, line 8 defines the substituent A as benzene, naphthalene, 5,6,7,8-tetrahydronaphthalene, quinoline, isoquinoline, indole or 7-azaindole; R₁ as -H, -CN, -SO₃R₄, -SO₂NHR₅, etc.; R₂ as C₁-C₆ alkyl, halogen, or hydroxy; R₃ as -H or C₁-C₆ alkyl; and q as zero, 1 or 2. Compounds of the instant invention are generically embraced by US '135 in view of the interchange ability of R₁, R₂, R₃, q and A substituents of the azaindolin-2-one ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example A is indole as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Claims 1-5, 9, 11, 12, 16, 19-37 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al., WO 96/16964 (US equivalent 5,719,135). The generic

Art Unit: 1624

structure of US '135 encompasses the instantly claimed compounds (see Formula I, column 1) and for the same use as claimed herein. Examples 53-71 of US '135 are position isomers of the compounds of the instant invention where compounds such as compound 52 in column 4 has the A variable attached at the 3-position of the indolyl ring attached to the azaindolin-2-one ring through methenylene. One of ordinary skill in the art at the time the invention was made would have been motivated to substitute the instantly claimed isomer for the known tyrosine kinase inhibitors of US '135. Such modification would be obvious because such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. (See *In re Norris*, 84 USPQ 459, on the obviousness of structural isomers).

Allowable Subject Matter

11. Claim 18 is allowed. None of the prior art of record nor a search in the pertinent art area teaches the species as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Monday thru Friday from 9:00 AM to 5:30 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Art Unit: 1624

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Richard L. Raymond
RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624

BC

Brenda Coleman
March 15, 2000